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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/386,266	BRAYDEN, DAVID J.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,15-20 and 35-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,15-20 and 35-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 10/08/03 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 10/08/03 in response to the final Office Action mailed 05/02/03.

Status of Claims

3) Claims 1 and 15 have been amended via the amendment filed 10/08/03.

New claims 35-46 have been added via the amendment filed 10/08/03.

Claims 1-6, 15-20 and 35-46 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

6) Claims 1-6 and 15-20 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 15, as amended, now replace previous the limitation: "at least 50% of the microparticles are at least 0.6 μm and at least 50% of the microparticles are less than 5 μm" with --at least 50% of the microparticles are greater than 0.6 μm and at least 50% of the microparticles are

less than 5 μm--. Applicants state that claims 1 and 15 are amended to replace the limitation 'at least 0.6 μm' with the limitation 'greater than 0.6 μm'. Applicants assert that there is descriptive support for the claimed numerical range 'greater than 0.6 μm and less than 5 μm'. Applicants point to page 5, line 13 to page 6, line 2 of the specification as providing descriptive support for the new limitations. Applicants contend that the present application discloses two distinct subsets of particles: microparticles and nanoparticels, and requires that microparticles and nanoparticles each elicit two different polarized immune responses: T_H1 and T_H2, respectively. Applicants state that use of microparticles implies a polarized T_H1 response while use of nanoparticles implies a polarized T_H2 response and that it is not possible to simultaneously have a polarized T_H1 response and a polarized T_H2 response. Applicants submit that since the two polarized immune responses are mutually exclusive, it follows from the specification on page 5, line 13 to page 6, line 2 that microparticles and nanoparticles are mutually exclusive subsets of particles. Applicants contend that 'a microparticle cannot be a nanoparticle and vice versa'. Applicants state that the particles of the application are defined by their median sizes in that administration of particles with a median size 'less than or equal to 600 nm (0.6 μm)' would induce a T_H2 response, thus making such particles nanoparticles. Applicants state that the median size of the T_H1-inducing microparticles must be 'less than or equal to 5 μm'. Applicants further state that because a polarizing T_H1-inducer cannot be a polarizing T_H2-inducer, a microparticle cannot be a nanoparticle. Applicants argue that because nanoparticles have a median size less than or equal to 0.6 μm, microparticles must have a median size greater than 0.6 μm. Applicants conclude that upon a careful reading of the specification, one of skill in the art could come to no other conclusion. Applicants further make the following statement:

> The fact that the median size of the T_H1-inducing microparticles must be greater than 0.6 μm is an inherent characteristic of the T_H1-inducing microparticles, and need not be stated explicitly.

Applicants then cite MPEP 2163.07(a) and conclude that no extrinsic evidence is necessary to establish inherency. Applicants state that it is an inherent characteristic of T_H1-inducing microparticles that their median size is greater than 0.6 μm. Applicants insist that because 'this is an inherent characteristic of T_H1-inducing microparticles, applicant submits that the recitation 'greater than 0.6 μm' is not new matter". Applicants assert that Applicant may combine the upper limit of 5 μm with the clearly delineated lower limit of 600 nm (0.6 μm) given the teaching in the specification

that particles with a median size 'greater than 600 nm (0.6 μm) induced a T_H1 response'. Applicants point to the original claim 7, which allegedly made clear that 600 nm was the upper limit for a T_H2 response. Applicants cite MPEP 608.01(1) and assert that whether or not claim 7 is non-elected in irrelevant. Applicants contend that the term 'particle' is used generically to describe the particles greater than and less than 600 nm on page 19 of the application. Applicants point to page 19, line 23 to page 20, line 1 of the specification as indicating that particles greater than 600 nm (0.6 μm) were made and could be identified using SEM analysis.

Applicants' arguments have been carefully considered, but re non-persuasive for the following reasons. It is important to take a look at claim 1 or claim 15, as it got amended during the course of the prosecution thus far. For example, Claim 1, as originally presented, is reproduced below, which did not include a lower and an upper limit for the microparticle size:

> 1. A method of inducing a T_H1 polarised immune response to an antigen, comprising parenterally administering to a subject microparticles sized such that **at least 50% of the microparticles are less than 5 μm**, the microparticles comprising the antigen entrapped or encapsulated by a biodegradable polymer. [Emphasis added].

Instead, microparticles having any size as long as the size is less than 5 μm were described/recited as inducing a T_H1 polarised immune response. The original claim 1 did not include a range with an upper size limit and a lower size limit. The term 'less than 5 μm' in the original claim included every size up to 5.0 μm and did not exclude microparticles of less than 0.6 μm size from inducing the recited T_H1 polarised immune response.

In response to the art rejections made in the Office Action mailed 04/23/02, claim 1 was amended via the amendment filed in September 2002. The amended claim 1 is reproduced below:

> 1. A method of inducing a T_H1 polarised immune response to an antigen, comprising parenterally administering to a subject microparticles sized such that at least 50% of the microparticles are **at least 0.6 μm** and at least 50% of the microparticles are less than 5 μm, the microparticles comprising the antigen entrapped or encapsulated by a biodegradable polymer. [Emphasis added].

This amendment to claim 1 placed a lower limit only for a part of the microparticles, i.e., for those microparticles that are at least 0.6 μM in size. The other at least 50% of microparticles less than 5 μm in size could still include microparticles less than 0.6 μM in size. At the time, Applicants pointed to 'Claim 1 vs. Claim 7' as filed, and page 5, third paragraph vs. fourth paragraph for support.

Applicants at the time stated that the 'claims in the application as filed incompletely reflected the distinction'. Consistent with the Office's position on new matter, via the amendment filed 09/23/02, Applicants further acknowledged that the 'claims set an upper limit (5 μM) to the median size of a microparticle population, but *failed to set a lower limit*' [Emphasis added]. There was no mention of an inherent support.

In response to the new matter rejection made in the Office Action mailed 11/29/02, Applicants amended claim 1 via the amendment filed in October 2003. The currently amended claim 1 is reproduced herebelow:

> 1. A method of inducing a T_H1 polarised immune response to an antigen, comprising parenterally administering to a subject microparticles sized such that at least 50% of the microparticles are **greater than 0.6 μm** and at least 50% of the microparticles are less than 5 μm, the microparticles comprising the antigen entrapped or encapsulated by a biodegradable polymer. [Emphasis added].

Applicants now make an inherency argument that the median size of greater than 0.6 μm is an inherent characteristic of T_H1-inducing microparticles is not persuasive. However, the novelty of a particular invention has to be fully described/disclosed, fully enabled and distinctly claimed. While a functional property of a product can be argued to be inherently present in a disclosed product, the structural limitations, such as, a particle size or size range cannot be asserted to be inherently present, especially after the explicit admission that the specification/claims, as filed, 'set an upper limit (5 μM) to the median size of a microparticle population, but *failed to set a lower limit*'. The specification on page 5, line 13 to page 6, line 2 is not supportive of the now recited range and its association with induction of a polarised T_H1 immune response. The general description on page 19, line 23 to page 20, line 1 of the specification with regard to making and identifying of particles greater than 600 nm (0.6 μm) using SEM analysis does not provide support for the claimed method of 'inducing a T_H1 polarised immune response to an antigen' by administering the microparticles of the recited size range. A method of inducing a polarized T_H1 immune response to an antigen by parenterally administering to a subject microparticles with the now recited microparticle size range is not contemplated in the instant specification, as originally filed. Therefore, the new limitations in the instant claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step

from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the limitation identified above, or to remove the new matter from the claim(s).

7) Claims 35, 36, 41, 42 and those that depend therefrom are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claims 35 and 41 recite microparticles having a diameter range of: 'from about 2.2 μm to about 4.3 μm' whereas new claims 36 and 42 recite a specific size of 'less than 3 μm' within this range. Applicants point to lines 13-21 on page 5; lines 5-9 on page 15 and lines 19 and 20 on page 16; Tables 1 and 2 as well as original claims 1-5 and 15-20 as providing support for the new claims 35-46. However, a review of the specification shows that lines 13-21 on page 5 and Tables 1 and 2 do not provide descriptive support for microparticles of the specific size range: 'from about 2.2 μm to about 4.3 μm' and for microparticles that are 'less than 3 μm' within size the range of 'from about 2.2 μm to about 4.3 μm'. Lines 5-9 on page 15 and lines 19 and 20 on page 16 support microparticles having an average diameter of 2.2 μm, but not the recited range. The original claims 1-5 and 15-20 are not supportive of the microparticles having the now recited size range. Therefore, the new limitations in the instant claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the limitation identified above, or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 102

8) Claims 1-4, 6 and 15-18 are rejected under 35 U.S.C § 102(b) as being anticipated by Maloy *et al.* (*Immunology* 8: 661-667, 1994).

Maloy *et al.* taught a method of inducing DTH responses (i.e., polarized T_H1 immune

response) to ovalbumin antigen comprising parenteral administration to a subject of a vaccine formulation comprising ovalbumin antigen entrapped in PLG microparticles sized 660 nm. The antigen was contained in a carrier, such as, saline or Quil A (see abstract; Materials and Methods; and Results). The micropaticles of particle size 660 nm meets the instantly recited size of the microparticles, since 0.66 μm is greater than 0.6 μm and also less than 5.0 μm or less than 3.0 μm. The PLG polymer comprises lactide and glycolide; and the microparticles are formed using solvent evaporation method (see page 662, left column). The administration of the composition was into the footpad of mice or by intraperitoneal route (see page 662). The method induced a strong ovalbumin-specific T-cell, CTL and DTH responses, i.e., T_H1 immune responses (see abstract; Figure 2-4; and Results). Maloy *et al.* taught that this most novel finding of induction of antigen-specific CTL responses after parenteral administration was never demonstrated previously using PLG microparticles (see Discussion on page 665).

Claims 1-4, 6 and 15-18 are anticipated by Maloy *et al.*

9) Claims 1-4, 6 and 15-18 are rejected under 35 U.S.C § 102(b) as being anticipated by Nixon *et al.* (*Vaccine* 14: 1523-1530, 1996 - already of record) as evidenced by Garcon *et al.* (US 6,372,227, already of record) or Rook *et al.* (US 6,056,964, already of record).

It is noted that the instant specification on page 11, lines 3-6 describes that T_H1 polarized immune response is characterized by the determination of specific IFN-gamma and IL-2.

Nixon *et al.* taught a method of parenteral administration to mice of a composition comprising a microbial peptide antigen entrapped in microparticles comprising poly(lactide-co-glycolide) polymers, sized 2 μm (i.e., greater than 0.6 μm and less than 3 μm or 5 μm). The composition elicited a cytotoxic T cell activity (CTL) (see abstract; and page 1527; and Figure 4B). That the microparticles were formed by solvent evaporation is evident from the description provided under the section 'Microparticles' on page 1524. Mice were immunized i.p. or intraperitoneally, or s.c. or subcutaneously (i.e., parenterally) with microgram amounts (i.e., pharmaceutically effective amounts) of the microparticulate immunogen (i.e., entrapped or encapsulated immunogen) suspended in PBS (i.e., pharmaceutically acceptable carrier). See page 1524, right column under 'Immunization and *in vitro* CTL stimulation'; and Figure 4 legend. Nixon *et al.* expressly suggested having, in a vaccine composition, microparticles prepared from combinations of polymers designed

to degrade at different rates after immunization (see page 1530, second full paragraph). Nixon *et al.* expressly taught that microparticles can be used to deliver a mixture of multiple immunogens in a single shot (see page 1529, left column, lines 3-6).

That the prior art method induced T_H1 polarised immune response to the peptide antigen is inherent from the teachings of Nixon *et al.* in light of what is known in the art. For instance, Garcon *et al.* taught that CTL induction correlates with Th-1 cytokine profile responses, specifically IFN-gamma and IL-2 secretion (see lines 37-39 in column 1). Similarly, Rook *et al.* taught the association between TH1 response, production of IL2, IFN-gamma and CTLs and down-regulation of TH2 cell production, and the generation of CTLs driven predominantly by TH1 responses (see column 1, lines 20-24; and column 2, first full paragraph). The disclosure of Nixon *et al.* anticipates the instant claims. Garcon *et al.* or Rook *et al.* is **not** used as a secondary reference in combination with Nixon *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Nixon *et al.* See *In re Samour* 197 USPQ 1 (CCPA 1978).

The induction of a TH1 polarized immune response by the prior art vaccine in the method disclosed is inherent from the teaching of Nixon *et al.* Although the prior art reference does not expressly recite the induction of a TH1 polarized immune response by the vaccine in the disclosed method, the vaccine formulation and the method of Nixon *et al.* are viewed as the same as the instantly claimed vaccine formulation and method. Since the prior art vaccine formulation is structurally the same as the formulation recited in the instant claims and since the prior art method of parenteral administration of the vaccine formulation is the same as the instantly claimed method, the prior art formulation and the method are expected to, or necessarily result in the same effects, i.e., induction of a T_H1 polarized immune response to the antigen.

Claims 1-4, 6 and 15-18 are anticipated by Nixon *et al.*

Rejection(s) under 35 U.S.C. § 103

10) Claims 5 and 19 are rejected are rejected under 35 U.S.C § 103(a) as being unpatentable over Nixon *et al.* (*Vaccine* 14: 1523-1530, 1996, already of record) as applied to claims 1 or 15 above and further in view of Cahill *et al.* (*Vaccine* 13: 455-462, 1995, already of record) and Mills *et al.* (*Infect. Immun.* 61: 399-410, 1993, already of record).

The teachings of Nixon *et al.* are explained above which do not disclose the use of a *B.*

pertussis antigen entrapped or encapsulated in their biodegradable polymer and a method of its administration.

However, Cahill *et al.* demonstrated that *B. pertussis* FHA antigen stimulates a T-cell response on intraperitoneal immunization of mice and shows IL-2 secretion indicative of Th1 type response. Cahill *et al.* taught that the intraperitoneal immunization led to the secretion of low levels of IL-5 (see abstract).

The critical role of Th1 immune response in protective immunity to whooping cough and the need for induction of such a response to *B. pertussis* antigen(s) was also well known in the art. For instance, Mills *et al.* taught *B. pertussis* antigen(s) and the need for inducing cellular immune responses mediated by Th1 cells to elicit protective immunity to *B. pertussis* infection (see 'Materials and Methods' and first paragraph under 'Discussion').

It would have been *prima facie* obvious to one of ordinary in the art at the time the invention was made to replace Nixon's microbial antigen with Cahill's Th1 response-inducing *B. pertussis* FHA antigen to produce the instant invention, with a reasonable expectation of success. Given the central or critical need for inducing Th1 protective immune response against *B. pertussis* infection as explicitly taught by Mills *et al.*, one of skill in the art would have been motivated to produce the instant invention for the expected benefit of inducing a stronger or additive Th1 immune response to Cahill's *B. pertussis* antigen. Substitution of one microbial antigen with another, art-known microbial antigen which has been demonstrated in the art to induce Th1 response and low levels of IL-5 response on parenteral administration, would have been well within the realm of routine experimentation, would have been obvious to a skilled artisan, and would have brought about similar effects or results.

Claims 5 and 19 are *prima facie* obvious over the prior art of record.

11) Claims 20 are rejected under 35 U.S.C § 103(a) as being unpatentable over Nixon *et al.* (*Vaccine* 14: 1523-1530, 1996, already of record) as applied to claim 15 above and further in view of Jones *et al.* (*J. Biotechnol.* 44: 29-36, 1996, already of record).

The teachings of Nixon *et al.* are explained above which do not disclose a vaccine composition having microparticles with at least two subpopulations of microparticles comprising different antigens.

However, as set forth above, Nixon *et al.* expressly suggested having in a vaccine composition microparticles prepared from combinations of polymers designed to degrade at different rates after immunization (see page 1530, second full paragraph). Nixon *et al.* also expressly taught that microparticles can be used to deliver a mixture of multiple immunogens in a single shot (see page 1529, left column, lines 3-6).

The concept of using combined PLG encapsulated antigens was well known in the art. Jones *et al.* (1996) taught the possibility of combining vaccine components by individually mixing PLG encapsulated antigens. Jones *et al.* (1996) taught that this might overcome the problems of perturbations in the immune responses that have been observed during the development of combination vaccines for the simultaneous administration of immunogens from the same syringe. Jones *et al.* (1996) further disclosed that formation of antigens in polymers of different compositions and therefore, different decay rates would have the effect of programming primary and secondary doses into a single administration. Jones *et al.* (1996) taught the application of PLG microencapsulation of antigens for combination of vaccine components and stated that combination of vaccines comprising any number of antigens could be tailored to meet any requirement (see page 30, right column, lines 7-25).

It would have been *prima facie* obvious to one of ordinary in the art at the time the invention was made to use two subpopulations of Nixon's microparticles and entrap more than one antigen in these microparticles to produce the composition of the instant invention, with a reasonable expectation of success, because Jones *et al.* (1996) expressly taught that PLG microcapsules comprising any number of antigens could be combined to produce encapsulated combination vaccines, and Nixon *et al.* expressly suggested the use of combinations of polymers designed to degrade at different rates after immunization and the use of microparticles to deliver a mixture of multiple immunogens. One skilled in the art would have been motivated to produce the instant invention for the expected benefit of effectively and advantageously programming primary and secondary doses having different decay rates in a single composition as taught by Jones *et al.* (1996) and for delivering a mixture of multiple immunogens in a single shot as taught by Nixon *et al.*

Claim 20 is *prima facie* obvious over the prior art of record.

Relevant Prior Art

12) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- In the art of microencapsulation technology, the particle size is referred to in micrometers or nanometers wherein 1000 nm = 1 micrometer (see the last sentence on page 215 of O'Hagan. *In*: *New Generation of Vaccines*. (Ed) M.M. Levine. Marcel Dekker, Inc., Chapter 17. 2nd Edition, pages 215-228, 1997).

Remarks

13) Claims 1-6, 15-20 and 35-46 stand rejected.

14) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

15) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347 or (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909 or (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. DEVI, PH.D.
PRIMARY EXAMINER

December, 2003